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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,667	05/11/2007	Erik de Vries	I - 2003.010 US	2304
31846 7590 12/26/2007 INTERVET INC. PATENT DEPARTMENT PO BOX 318 MILLSBORO, DE 19966-0318			EXAMINER OGUNBIYI, OLUWATOSIN A	
			ART UNIT 1645	PAPER NUMBER
			MAIL DATE 12/26/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/571,667	Applicant(s) DE VRIES ET AL.	
	Examiner Oluwatosin Ogunbiyi	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,7-14 and 16-25 is/are pending in the application.
- 4a) Of the above claim(s) 14 and 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,7-13,16 and 21-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>5/2/06 and 3/14/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 4, 7-14 and 16-25 are pending in the application. Claims 2, 3, 5, 6 and 15 are cancelled. Claims 1, 4, 7-13, 16, 21-25 (all in part) are under examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Specification

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 11 for example.

The abstract of the disclosure is objected to because of legal phraseology such as said. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Appropriate correction is required.

Information Disclosure Statement

The information disclosure statements filed 5/2/06 and 3/14/06 have been considered. Initialed copies are enclosed.

Election/Restrictions

Applicant's election without traverse of Group I claims 1, 4, 7-13, 16 and 21-25 drawn to SEQ ID NO: 2 in the restriction requirement filed 11/13/07 is acknowledged.

Claims 14 and 17-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1,4,7-13 and 21-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to a Piroplasmid protein comprising, SEQ ID NO: 2 or immunogenic fragments of SEQ ID NO: 2.

As claimed, the invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. The recitation of "isolated" provided there is support for such recitation in the specification would reflect the hand of man.

Claim 16 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial and credible utility or a well established utility.

The invention is drawn to a prophylactic treatment of an infection caused by a Piroplasmid organism comprising administering a vaccine comprising a protein according to claim 1.

The prevention of infection caused by a Piroplasmid organism is not credible. Prevention of infection means that a single organism does not enter into tissues or cells of a subject's body. Prophylactic treatments e.g. vaccines for many infections kill the organism once it infects tissues or cells thus preventing disease due to said infections but such treatments do not prevent the organism from infecting in the first place. Prevention of infection is a very high bar because the vaccine must prevent at least one Piroplasmid from infecting a cell. Also, prevention of infection is different from prevention of disease caused by an infection as prevention of disease is prevention of symptoms due to an infection while preventing infection is inhibition of the infectious organism from invading or entering, for example, the human body, tissue, cells in the first place. Vaccines against a Piroplasmid organism such as Babesia afford protection due to lower parasitemias i.e. reduced infection (WC Brown et al. Parasitol Today. 1999 Jul;15(7):275-81, p. 275 right column first sentence). In immunized animals, infection by Piroplasmid organism occurs but because the immune system is primed, the animal is able to immunologically fight said organism (WC Brown et al p. 276 fig.1).

In summary, it would be reasonable to conclude that the utility of the instant claim i.e. to prevent infection would not credible utility based on the evidence of record.

Claim 16 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial and credible

utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention (see rejection below).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1,4, 7-13, 16, 21-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a Piroplasmid protein comprising, SEQ ID NO: 2 or immunogenic fragments of SEQ ID NO: 2 wherein said protein inhibits invasion of an

organism of the family Piroplasmida. The claims are also drawn to a vaccine comprising said SEQ ID NO:2 or immunogenic fragments and also a prophylactic or therapeutic treatment of an infection or its clinical signs caused by a Piroplasmid organism comprising administering a vaccine comprising a protein comprising SEQ ID NO:2 or immunogenic fragments thereof.

The nature of the invention is the inhibition of invasion of any organism of the family of Piroplasmida using SEQ ID NO:2 or immunogenic fragments thereof. The nature of the invention is also a vaccine and a prophylactic or therapeutic treatment of an infection or its clinical signs caused by a Piroplasmid organism.

As to the inhibition of invasion of an organism of the order of Piroplasmida by SEQ ID NO:2 or immunogenic fragments thereof, the specification teachings are limited to in vitro inhibition of *Babesia Bovis* from invading erythrocytes by antisera raised against fragments of SEQ ID NO:2. The specification on p. 30 teaches peptides from SEQ ID NO:2 (SEQ ID NO:2 is isolated from *Babesia bovis*) and immunization of rabbits with said peptides. On p. 33 and p. 35, the specification teaches inhibition of in vitro invasion by peptide-specific antisera in a *B. bovis* in vitro invasion assay. The specification does not correlate inhibition of invasion of *Babesia bovis* or other organisms of the order/family of Piroplasmida with SEQ ID NO:2 or immunogenic fragments thereof. The order of Piroplasmida is broad and comprises several organisms that belong to said order (see p. 5 lines 24-28). The specification does not provide a working example of the inhibition of invasion of even one of all these organisms by SEQ ID NO: 2 or immunogenic fragments thereof. The specification is devoid of any in vitro or in vivo evidence that SEQ ID NO:2 or immunogenic fragments thereof inhibits the invasion of any organism of the order of Piroplasmida. As mentioned above the specification teachings are limited to in vitro inhibition of invasion by antisera raised to

peptide fragments of SEQ ID NO: 2. It is unpredictable that SEQ ID NO: 2 or immunogenic fragments thereof can inhibit invasion of Piroplasmida in an in vitro invasion assay similar to that described in the specification for inhibition of invasion by peptide specific antisera.

As to a vaccine or any other prophylactic treatment comprising SEQ ID NO: 2 or immunogenic fragments thereof the specification does not correlate SEQ ID NO: 2 or immunogenic fragments thereof with a protective immune response against any Piroplasmid organism. There is no challenge data in animal model that provides evidence for a vaccine or prophylaxis (prevention) against infection by Piroplasmid organisms. The specification teaches that peptide fragments of SEQ ID NO: 2 are immunogenic; however immunogenicity does not translate to a protective immune response.

Vaccines induce protection against infections by stimulating the development of long-lived effector cells and memory cells (Abbas et al. Chapter 15 p. 360-362). Vaccines by definition trigger an immunoprotective response in the host vaccinated and mere antigenic response is insufficient. It is well recognized in the vaccine art, that it is unclear whether an antigen(s) derived from a pathogen will elicit protective immunity. Ellis, R.W. (Chapter 29 of "VACCINES" [Plotkin, S.A. et al. (eds) published by W. B. Saunders company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.... and thus protect the host against attack by the pathogen". In the instant case, the specification has not correlated the production of protective antibodies via active immunization with the claimed proteins with protection against any Piroplasmida organism in order to result in a

vaccine or prophylactic treatment of an infection. Further, the specification does not correlate the administration of SEQ ID NO: 2 with therapeutic treatment of ongoing infection with any Piroplasmid organism.

The *Babesia bovis* vaccine art at the time the instant invention was made teaches that attempts being made to develop subunit vaccines have been slow (De Vos et al. Ann N Y Acad Sci 2000; 916:540-5). Further serologically immunodominant antigens are usually not protective (WC Brown et al. Parasitol Today. 1999 Jul;15(7):275-81, p. 278 column 1 last paragraph, MC Jenkins, Veterinary Parasitology 101 (2001): 291-310 p. 300 first paragraph). Preliminary results suggest that vaccines based on single antigens do not confer an adequate level or duration of protection, and it is likely that a vaccine based on a single antigens will be need to induce adequate protection (De Vos et al. Ann N Y Acad Sci 2000; 916:540-545 p. 544).

In the instant case, it is unpredictable whether the instantly claimed proteins can elicit a protective immune response commensurate with the scope of the claims i.e. a vaccine/prophylactic. The protective efficacy of the claimed proteins is unpredictable in light of the lack of guidance or an example correlating an immune response generated by this protein with protection against any Piroplasmid organism.

In view of the above undue experimentation would be required of the skilled artisan to use the instant invention as claimed.

Claims 1, 4, 7-13, 16, 21-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 1, the recitation of "...said protein inhibits invasion of an organism of the family of Piroplasmida" is confusing. As claimed it is not clear what is being invaded. Is an organism of the family Piroplasmida being invaded?

Claim 9 is drawn to a live recombinant carrier comprising i) a nucleic acid according to claim 4, ii) a cDNA fragment comprising (i), iii) a recombinant DNA molecule comprising (i), or iv) a recombinant DNA molecule comprising (ii); wherein said cDNA fragment or said nucleic acid is under the control of a functionally linked promoter.

Claim 10 is drawn to a host cell comprising i) a nucleic acid according to claim 4, ii) a cDNA fragment comprising (i), iii) a recombinant DNA molecule comprising (i), iv) a recombinant DNA molecule comprising (ii), v) a live recombinant carrier comprising (i), vi) a live recombinant carrier comprising (ii), vii) a live recombinant carrier comprising (iii), or viii) a live recombinant carrier comprising (iv); wherein said nucleic acid or said cDNA fragment are under the control of a functionally linked promoter.

As written the metes and bounds of the product of claims 9 and 10 are not clear. It appears that the live recombinant carrier comprises items all of items i-iii or all of items i-ii and iv. Similarly, it appears that the host cell comprises all of items i-vii or all of items i-vi and viii. Alternatively, the references to different alternatives within alternatives renders the metes and bounds of the live recombinant carrier and the host cell unclear.

Status of the Claims

Claims 1, 4, 7-13, 16, 21-25 are rejected. No claims allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Examiner Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Oluwatosin Ogunbiyi

Examiner

Art Unit 1645



PATRICIA A. DUFFY
PRIMARY EXAMINER